UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/745,605	12/22/2000	Gary C. Starling	DB13NP; 30436.43USU1	1201

23914 7590 03/25/2005

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS

AND INTERFERENCES

Paper No. 20050313

Application Number: 09/745,605

Filing Date: December 22, 2000

Appellant(s): STARLING ET AL.

Keith R. Lange

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed January 22, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences, which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment filed 8/20/03 and the Declaration under 37 C.F.R 1.131 has been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct. However, claims 2-4 were found to satisfy the written description requirements. Therefore, claims 2-4 are hereby withdrawn from the rejection under issue D.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims stand or fall together for the sole purpose of allowing the Board to select a single claim for review, and to decide the appeal as to the grounds of rejection on the basis of that claim alone.

(8) ***Claims Appealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) ***Prior Art of Record***

Attwood TK, Science 290(5491) :471-473, 2000.

Skolnick et al. Trends Biotechnol. 18(1) :34-39, 2000.

Metzler et al. Nature Structural Biol. 4 :527-531, 1997.

Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495.

Meinkoth *et al* in Analytical Biochemistry, 138:267-284, 1984).

(10) ***Grounds of Rejection***

The following grounds of rejection are applicable to the appealed claims:

Issue A: **Indefinite/35 U.S.C 112, second Paragraph.**

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "hybridizes under stringent conditions" in claim 54 is ambiguous. Although the specification discloses on pages 31-32 general parameters for calculating such conditions, it is unclear which conditions are actually claimed.

Issue B: **Utility/35 U.S.C. § 101**

10. Claims 1-5 and 53-65 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

Appellant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The instant application has provided a description of an isolated nucleic acid encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of the protein or its significance. The instant specification asserts that the protein may be a potential target for disease such as inflammation, cancer, and immune disorders (page 54, lines 5-6). The specification asserts that arteriosclerosis, asthma, autoimmune anemia, acquired immunodeficiency syndrome (AIDS), bursitis, cholecystitis, cirrhosis, crohn's disease, atopic dermatitis, diabetes, mellitus, emphysema, atrophic gastritis, inflammatory bowel disease, multiple sclerosis, myasthenia gravis, myocardial or pericardia inflammation, osteoarthritis, osteoporosis, psoriasis, Reiter's syndrome, rheumatoid arthritis, and systemic lupus erythematosus (page 54, lines 21-28) could be treated or prevented by administration of a therapeutically effective amount of APEX or an agonist thereof. The specification also asserts that administration of a therapeutically effective amount of APEX or an agonist thereof could treat or prevent cancer such as adrenal gland, bladder, bone, bone marrow, breast, cervix, gall bladder, gastrointestinal tract, kidney, liver, lung, muscle, ovary, pancreas, prostrate, salivary glands, skin, spleen, testis, thymus, thyroid and uterus (page 54, lines 29-31 and page 55 line1).

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the CD2 subfamily- similar protein (APEX). The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially

useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The instant claims are drawn to a nucleic acid encoding a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion CD2 subfamily-like protein (APEX) of the instant application was, as of the filling date, useful for regulating adhesion and generating co-stimulatory signals to mediate leukocyte proliferation, differentiation, migration, or activation (page 16, lines 11-18). Until some actual and specific significance can be attributed to the protein identified in the specification as APEX, or the gene enoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The nucleic acid of the instant invention and the protein encoded thereby are compounds which share some structural similarity with CD2 subfamily based on sequence similarity. The CD2 subfamily includes CD2, CD58, CD48, CD59, CD84, Ly9, 2B4, and CDw150 (SLAM). These proteins share several common structural domains such as extracellular Ig-like domains, a transmembrane domain or a glycosylphosphatidylinositol (GPI)-anchor moiety. CD84 and Ly9 functions have not been elucidated to date while SLAM has been shown to enhance antigen-specific proliferation and cytokine production by CD4+ T cells. It is not clear if the protein of the instant application would have the same function to enhance antigen-specific proliferation and cytokine production. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the

multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentablility. Since the instant specification does not disclose a credible "real world" use for APEX, then the claimed invention as disclosed does not meet the requirement of 35 U.S.C. § 101 as being useful.

Issue C: ***enablement/35 U.S.C § 112, first paragraph***

11. Claims 1-5 and 53-65 are also rejected under 35 U.S.C. § 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, besides an isolated nucleic acid molecule of SEQ ID NO: 1 encoding amino acid SEQ ID NO: 4 the specification fails to provide any guidance as to how to make any isolated nucleic acid molecule encoding APEX-1 in claim 1; any isolated nucleic acid molecule wherein APEX-1 has an extracellular domain encoded by nucleotide sequences beginning with thymine (t) at position 108 and ending with cytosine (c) at position 716 in claim 5; any isolated variant having at least 70% polynucleotide sequence identity to the isolated nucleic acid molecule encoding APEX-1 in claim 53; any isolated polynucleotide which hybridizes under stringent conditions to

the complement of polynucleotide encoding APEX-1 in claim 54; or any nucleic acid molecule comprising a nucleotide sequence which is complementary to the isolated nucleic acid molecule encoding APEX-1 in claim 55. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only a single nucleic acid sequence (SEQ ID NO:1) encoding a single polypeptide (SEQ ID NO:4). The instant claims encompass in their breadth *any* nucleic acid encoding a polypeptide (nucleic acid encoding APEX-1); or *any* nucleic acid that "hybridizes under stringent conditions"; or nucleic acids variants (with at least about 70% polynucleotide sequence identity).

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences.

The term "has" in claim 5 is open-ended and extend the APEX to encode additional undisclosed amino acid sequences. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Because of the lack of sufficient guidance and predictability in determining which modifications would lead to the same structure of a nucleic acid encoding APEX-1. Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of sufficient guidance and working examples, predicting what changes can be made to the amino acid sequence of SEQ ID NO: 4 that after modification will retain the same structure of APEX-1 protein is unpredictable. The instant claim language

encompass fragment. For example, claims 5 recites an isolated nucleic acid wherein APEX-1 has an extracellular domain. Such a recitation does not require that the nucleic acid encode the full length sequence set forth in SEQ ID NO:4; but rather encompasses *fragments* specially with open ended language as noted supra.

The fact that two nucleic acid sequences will hybridize under stringent conditions does not in and of itself require that the two sequences share any functional activity. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible with respect to the citation in claim 15 "variant having 70% polynucleotide sequence identity" in the absence of a clear recitation that the identity is over the full length of SEQ ID NO:1 the claim reads on fragments. Meinkoth *et al* in Analytical Biochemistry (138:267-284, 1984) indicate factors that affect nucleic acid hybridization such as probes length of the shortest chain in the duplex, the ionic strength , base composition and the concentration of the helix destabilizing agents (page 269, left column 2nd and 3rd paragraphs in particular).

The claims as written encompass a broad genus of polynucleotides with a large number of possibilities with regard to the length of the nucleic acid sequence. Further, making changes up to 30% of an nucleic acid sequence does not provide maintaining the same three dimensional structure as the 100% identity *over the full length of SEQ ID NO:1*. The instant claim language appears to encompass polynucleotide variants. For example, claims 53 and 54 recite a nucleic acid a variant having at least 70% polynucleotide sequence identity and a polynucleotide which hybridizes to an isolated nucleic acid molecule encoding APEX-1, respectively. Such a recitation does not require that the nucleic acid encode the full length sequence set forth in SEQ ID NO:1; but rather encompasses any nucleic acid sequence comprising either the full length of SEQ ID NO:1 or *any variant*. The specification does not appear to have provided any working examples of any variants. Thus it would require undue experimentation of the skilled artisan to determine which variants of SEQ ID NO:1 would identify nucleic acid of SEQ ID NO:1.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences and still encode a polypeptide is unpredictable, as is the identity of which variant would encode APEX-1; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Issue D: **written description /35 U.S.C § 112, first paragraph**

Claims 1, 5 and 53-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2-4 were found to satisfy the written description requirements. Claims 2-4 are hereby withdrawn from the rejection.

Appellant is in possession of nucleic acid molecule of SEQ ID NO: 1 encoding amino acid of SEQ ID NO:4.

Appellant is not in possession of make any isolated nucleic acid molecule encoding APEX-1 in claim 1; any isolated nucleic acid molecule wherein APEX-1 has an extracellular domain encoded by nucleotide sequences beginning with thymine (t) at position 108 and ending with cytosine (c) at position 716 in claim 5; any isolated variant having at least 70% polynucleotide sequence identity to the isolated nucleic acid molecule encoding APEX-1 in claim 53; any isolated polynucleotide which hybridizes under stringent conditions to the complement of polynucleotide encoding APEX-1 in claim 54; or any nucleic acid molecule comprising a nucleotide sequence which is complementary to the isolated nucleic acid molecule encoding APEX-1 in claim 55.

Appellant has disclosed only nucleic acid of SEQ ID NO: 1; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception in the above cases cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

A description of a genus of nucleic acid sequences may be achieved by means of a recitation of a representative number of the polynucleotide variants having 70% polynucleotide sequence identity; polynucleotide sequences which hybridizes under stringent conditions to complement of polynucleotide encoding APEX-1 or nucleic acid molecules wherein APEX-1 has an extracellular domain falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Issue E: **Anticipation/102(b)**

Claims 53-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al (GenBand Accetion No. H73135 (1995))

Hillier *et al* teach a 436 polynucleotide having 100% polynucleotide sequence identity to the polynucleotide at positions (49-306) of the claimed SEQ ID NO: 1. The reference polynucleotide is a sense sequence that would hybridize under stringent conditions to complement of polynucleotide encoding APEX-1. Claim 55 is included because complementary nucleic acids are intrinsic properties of the nucleic acid sequence because DNA strands are produced by copying preexisting DNA strand wherein the DNA from which the new strand is copied is called a template and the first copy has a complementary sequence. The term "having" in instant claim 53 is open-ended. It would open up the claim to include the reference 436 polynucleotide. In addition, the term "variant" in the instant claim 53 includes different forms of the gene including deletions and therefore, the claim reads on the reference nucleic acid sequence.

The reference teachings anticipate the claimed invention.

(11) Response to Argument

Issue A: **Indefinite**

Claims 54 allegedly points out and distinctly claims the subject matter which applicants regards as the invention, in satisfaction of 35 U.S.C 112, second paragraph.

Utility

At page 5, first paragraph of the Brief, Appellant submits that what is set forth is in the specification are specific hybridization conditions which are readily recognized by those of skill in the art to result in a clearly and readily detectable hybridization signal. Appellant points out to the specification on page 31, lines 5 and 10 which set forth stringent salt conditions are desirable less than about 250 mM NaCl and 25 mM sodium citrate and stringent temperature conditions are at least about 42°C, respectively. Appellant argue that one skilled in the art may readily look to the present specification for guidance to determine the scope of "stringent conditions" within the context of the present claims in order to determine under which conditions a clear hybridization signal may be obtained. Appellant submit that it is not necessary to recite each of the conditions set forth in the specification in place of the term "stringent conditions" in claim 54. Rather, what is required is that claim 54, read in view of the teachings of the specification of "stringent conditions" set forth in the specification.

This has been fully considered but is not found to be persuasive. The specification on page 31 provides general stringency conditions, wherein said conditions can vary in stringency, that is the conditions can be less than about 250 mM NaCl and 25 mM sodium citrates. The specification also discloses that the temperature conditions will normally include a temperature of at least about 30°C, more preferably at least about 37°C, and most preferably of at least about 42°C. Therefore, the ionic strength and temperature conditions provided in the specification also include low to moderate stringent conditions. Therefore, in the absence of a clear definition of the metes and bounds of this "stringent conditions" it is unclear which conditions are actually claimed.

Issue B: **Utility/35 U.S.C §101**

Claims 1-5 and 53-65, allegedly, are supported by specific and/or substantial asserted utility, in satisfaction of 35 U.S.C §101.

At page. 6, first paragraph of the Brief, Appellant characterizes the invention as nucleic acid molecules encoding APEX-1, polynucleotides having certain sequence identity to such nucleic acid molecules, polynucleotides which hybridize to the complement of such nucleic acid molecules, nucleic acid molecules encoding APEX-1, and host vector systems comprising such vectors. Appellant also states that APEX-1 polynucleotides of the present invention are homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation, and diseases associated therewith. Appellant further states that the claimed molecules therefore have uses similar to those of other members of the CD2 subfamily.

This has been fully considered but is not found to be persuasive. The specification does not disclose that the claimed genes are markers for specific diseases. Absent a disclosure of altered levels or forms of a gene in diseased tissue as compared with the corresponding healthy tissue, the gene is not a disease marker or an appropriate target for drug discovery or toxicology testing.

Specific and substantial Utility

At page. 6, last paragraph, Appellant refers to utility guidelines and states that if Appellants have asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, then the utility requirement of section 101 is satisfied. Appellant states that the present specification clearly sets forth both specific and substantial utility for the claimed invention. Appellant submits that APEX or an agonist thereof may be administered to treat any number of known disorders, including inflammatory, cancer and immune disorders. Further, Appellant states that it is well established that nucleic acids and

proteins encoded thereby, such as APEX, which are shown to be expressed in various tissues, may be biological targets for the treatment of disease states associated with such tissues.

This has been fully considered but is not found to be persuasive. The asserted utility is not specific or substantial. Since a defect in any polynucleotide or polypeptide is likely to cause a disease of some sort, every polynucleotide or polypeptide is a target for drug development. Thus, the asserted utility is not specific to the claimed APEX-1. Furthermore, the specification does not disclose a nexus between any specific disease states and a change in the amount or form of APEX genes. Significant further research would have to be conducted to identify such a nexus. Therefore, the asserted utility is not substantial.

Credible Utility

At page 7 of the Brief, Appellant argues that the present specification states repeatedly that the claimed invention shows homology to a well-characterized class, namely the CD2 subfamily. Appellant submits that the Examiner's reliance on Brenner is misplaced. Appellant submits that Brenner stands for the proposition that a claimed invention must have a practical utility (e.g., must not be useful solely for research purposes) and that utility is not satisfied merely by showing that a compound yielded belongs to a class of compounds which scientists are investigating for possible uses. In Brenner, the claimed process for making a steroid was found to lack utility because the resultant steroid did not have known utility. Appellant submits that the present invention is homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation and diseases associated therewith. Appellant asserts that the claimed molecules have the specific, substantial and credible uses set forth above. Appellant asserts that APEX genes have uses similar to those of other members of the CD2 subfamily.

This is not found persuasive because without some common biological activity for the family members, a new member would not have a specific, or substantial utility when relying only on

the fact that it has structural similarity to the other family members. The nucleic acid of the instant invention and the protein encoded thereby are compounds which share some structural similarity with CD2 subfamily based on sequence similarity. The CD2 subfamily includes CD2, CD58, CD48, CD59, CD84, Ly9, 2B4, and CDw150 (SLAM). These proteins share several common structural domains such as extracellular Ig-like domains, a transmembrane domain or a glycosylphosphatidylinositol (GPI)-anchor moiety. CD84 and Ly9 functions have not been elucidated to date while SLAM has been shown to enhance antigen-specific proliferation and cytokine production by CD4+ T cells. It is not clear if the protein of the instant application would have the same function to enhance antigen-specific proliferation and cytokine production. The members of the family have different biological activities, but there is no evidence that the claimed nucleic acid encoding APEX-1 polypeptide would share any one of those different activities. That is, no activity is known to be common to all members of CD2 subfamily. This case is analogous to *Brenner V. Manson*. Since some CD2 members are functional and some are non functional, therefore, a person of ordinary skill in the art could not impute utility based on a substantial likelihood. Further, one ordinary skilled in the art at the time the invention was made could not determine whether the expression of APEX-1 would mediate leukocyte proliferation, differentiation, migration or activation based multifunctional activity of CD2 subfamily. One of ordinary skilled in the art would be able to use such information for research to identify and characterize the encoded proteins of the invention. Such research has been determined by the courts to be a utility, which, alone, does not support patentability.

At page 8, sencond paragraph, Appelant submtis that under the presnt law, homology to a molecule it known utility is accdptable for extabishing section 101 utility. Fujikawa V. Wattanasin, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). Appellant concuded that under Fujikawa, homology of the inentive compounds to the CD2 subfamily which has known utility is sufficient to satisfy secton 101.

This is not found persuasive because CD2 is a multifunctional molecule that contributes significantly to T-cell adhesion and signal transduction. The CD2 subfamily to which the encoded polypeptide belongs is a family in which the members have divergent functions based

on which tissues the protein is expressed or to which it is administered. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. Further, the specification does not specify the degree of homology shared between the claimed nucleic acid and the CD2 subfamily members. The Examiner notes that the claimed nucleic acid molecule share only 34% sequence homology a member of CD2 subfamily.

At page 8, third paragraph, Appellant submits that it is not the law that compounds showing homology to claimed compounds cannot be classified in a family the members of which may have divergent function. Appellant asserts that their burden is simply to show that the claimed compounds either have demonstrated utility or can be shown to have homology to molecules, which have demonstrated utility. Appellant submits that the utility is established at the very least by the use of the claimed compounds as molecular weight markers.

This is found not persuasive because assignment to a prior art family of proteins is generally insufficient to meet the utility requirement unless such assignment would allow the artisan to assign a specific and substantial use to the new member of the protein family. In the absence of an understanding of the specific and substantial use for the claimed APE-1, the claimed nucleic acid molecule encoding the APEX-1 protein would not comply with the requirements for utility. That is, no activity is known to be common to all CD2 members. After further research specific and substantial utility might be found for the claimed isolated nucleic acid molecule. This further characterization, however, is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. Further, one of ordinary skill in the art must understand how to achieve a practical benefit from knowledge of the class, however, there is no practical benefit from use of the claimed invention because utility is not specific and substantial. Appellant have not identified a general utility, which is specific and substantial, which applies to the broad class of CD2 protein family. The asserted utility of that the claimed nucleic acid can be used as molecular weight markers is not specific. Since the same can be done with any nucleic acid molecule, this asserted utility is not specific to the claimed APEX-1 polynucleotides.

Issue C: **Enablement Rejection under 35 U.S.C. §112, first paragraph**

To the extent the rejection of the invention under 35 U.S.C. § 112, first paragraph, is based on the rejection for lack of utility under 35 U.S.C. § 101.

Claims 1-5 and 53-65 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

As Appellant asserts at p.8-9 of the Brief, the same arguments are set foth as to why the claimed invention has utility under section 101. Further, Appellant argues that one skilled in the art would readily be able to make and use the claimed compounds as set forth, for example, in the present specification. Appellant asserts that the claimed compounds may be used in conventional screening assays and may be administered in therapeutically useful compositions.

Therefore, for reasons set forth above, Appellant arguments have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and it is believed that the rejections should be sustained.

With respect to making the claimed invention, Appellant at p.9, second paragraph argues that conventional amplification and cloning techniques may readily be used to generate APEX-1.

Appellant points the specification at page 60, lines 25et seq. of the present specification. This is not found persuasive. While it is true that one skill in the art can make SEQ ID NO:1 encoding SEQ ID NO:4, the specification fails to provide any variant having at least 70% polynucleotide sequence identity to an isolated nucleic acid molecule encoding APEX-1, any isolated nucleic acid molecule encoding APEX-1 or any APEX-1 has an extracellular domain encoded by nucleotide sequences beginning with thymine (t) at position 108 and ending with cytosine (c) at position 716 of SEQ ID NO: 1. The specification fails to provide any polynucleotide which

hybridizes under stringent conditions to the complement of an isolated nucleic acid molecule encoding APEX-1. The enablement issues of making the nucleic acid molecules still remain because the specification does not teach and provide sufficient guidance as to which 30% of the nucleic acid molecule encoding APEX-1 would have been altered such that the resultant nucleic acid molecule would have retained the function of the starting APEX-1.

Issue D: **Written Description**

Claims 1, 5 and 53-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At pages 9 of the Brief, Appellant asserts that the specification describes APEX-1. as a molecule having the maino acid sequence set forth in SEQ ID NO: 4 and encoded by a nucleic acid having the sequence set forth in SEQ ID NO: 1. Appellant concluded that a claim to an APEX-1 molecule is clearly described, no representative number of species need be provide. With respect to claims directed to variants and polynucleotides with hybridize to complements of APEX-1, Appellant submits that one of skill in the art, using the extensive teachings in the present specification, would recognize Applicants to be in possession of such molecules. Appellant submits that such molecules are recognized as having the utility set forth with respect for APEX-1, and one of skill in the art will be capable of using the sequences set forth in the resent specification to identify variations thereof which are within the scope of the present invention.

This found not persuasive because the specification does not describe the variants and the fragments themselves. The Examiner notes that the claimed invention which is drawn to a genus is not adequately described in the specification since no representative number of species are disclosed and there is insufficient disclosure of relevant, identifying characteristics sufficient to describe the claimed polypeptides in such full, clear, concise and exact terms that a skilled

artisan would recognize appellant was in possession of the claimed invention. Further, the specification fails to provide relevant, identifying characteristics include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the appellant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001). Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed APEX-1 genus of variants, wherein the variants having at least 70% polynucleotide sequence identity to an isolated nucleic acid molecule encoding APEX-1 and an isolated polynucleotide which hybridizes under stringent conditions to the complement of said isolated nucleic acid molecule of APEX-1 which retain the features essential to the instant invention. *No such variants were made or shown to have activity. Only the polypeptide APEX-1 of SEQ ID NO:4 encoded by the nucleic acid molecule of SEQ ID NO: 1 are disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.*

Issue E: **Anticipation under 35 U.S.C 102(b)**

Claims 53-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al (GenBand Accetion No. H73135 (1995)).

Appellant at pages 10-11 submits that Hillier is not a sufficient prior art reference. The description and enabling disclosure requirement of 35 U.S.C 112, first paragraph, having developed definition through many years of case law and are applied as the minimum qualitative level required for a reference to be effective. In re Hoeksema, 399 F.2d 269, 273, 158 USPQ 596, 600 (CCPA 1969); In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962). Appellant indicates that it is well-established that in order for a reference to serve as prior art, it must demonstrate that the claimed invention was in the possession of the public as dictated by

the patent statute or case law, including containing a sufficient description of, and an enabling disclosure for, the claimed invention. Appellant submits that the reference must contain sufficient technical information to describe the claimed invention to a person of ordinary skill in the art to which the claimed invention pertains and to enable such a person to make and use the claimed subject matter, without requiring undue experimentation. Appellant argues that Hillier fails to satisfy these requirements. Appellant submits that Hillier is nothing more than a sequence of nucleotide bases about which nothing is known. Appellant asserts that it is no more relevant than would be a randomly computer-generated sequence of nucleotide bases that coincidentally have the same sequence as the claimed invention. With respect to the Examiner's position that Appellant does not provide objective evidence to distinguish the prior art (i.e., Hillier) from the claimed invention, Appellant is not clear as to how this is relevant. Appellant submits that the Examiner has only provided a sequence with no evidence that anything at all is known about this sequence, Hillier clearly is not an enabled prior art reference and , therefore, does not anticipate the claimed invention. Appellant indicates that if the sequence of Hillier was claimed in a patent application, it is undoubtful that the claim would be rejected for lack of enablement (amoung other things). Appellant addresses the citation of In re Spada by arguing that this is also not relevant as the Examiner does not address Applicants' arguments by stating how Hillier is a sufficient prior art reference (i.e. has utility and includes adequate written description and enabling disclosure) and meets the legal requirements necessary to be anticipatory under Section 102. Appellant points out that In re Spada is not on point in any event. The present invention does not concern a situation where a known compound is being claimed by including functional language to properties which were previously not appreciated. In such a case the claimed compound is anticipated by the known compound as the known compound necessarily has those same properties., Appellant argues that the known compound must have utility, be described and enabled in order to anticipate the claimed invention. Appellant submits that Hillier merely sets forth a sequence of no known utility, for which there is no written description of the sequence and for which no enabling disclosure is provided.

This is found not persuasive because a reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed in invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). See MPEP 2121.01. Further, Appellant does provide objective evidence to distinguish the prior art from the claimed invention. Further, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties appellant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Appellant does provide objective evidence to distinguish the prior art teachings from the claimed invention. Therefore, Hillier et al anticipate the claimed invention.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Maher Haddad, Ph.D.

Art Unit 1644

March 15, 2005

Conferees

Christina Chan

SPE, Art Unit 1644

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Anthony C. Caputa.

SPE, Art Unit 1646

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600